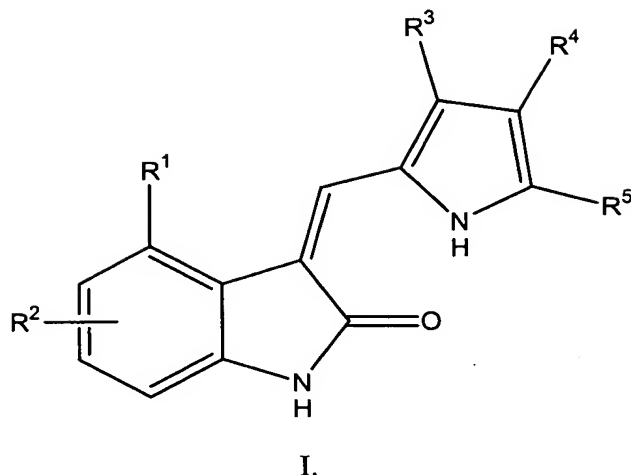


What is claimed is:

1. A compound of the formula I:



wherein:

$R^1$  is a heteroaryl substituent, optionally substituted by one or more substituent selected from the group consisting of halogen,  $-OR^6$ ,  $-COR^6$ ,  $-COOR^6$ ,  $OCOR^6$ ,  $-CONR^6R^7$ ,  $-R^6NCOR^7$ ,  $-NR^6R^7$ ,  $-CN$ ,  $-NO_2$ ,  $-CX_3$ ,  $-SO_2R^6$ ,  $-SO_2OR^6$ ,  $-SO_2NR^6R^7$ ,  $-R^6NSO_2R^7$ , perfluoroalkyl, lower alkyl, lower alkyl further substituted by one or more of  $R^2$ , lower alkenyl, lower alkenyl further substituted by one or more of  $R^2$ , lower alkynyl, lower alkynyl further substituted by one or more of  $R^2$ , cycloalkyl, cycloalkyl further substituted by one or more of  $R^2$ , heterocycle, heterocycle further substituted by one or more of  $R^2$ , aryl and aryl further substituted by one or more of  $R^2$ ;

$R^2$  is selected from the group consisting of hydrogen, halogen,  $-OR^6$ ,  $-COR^6$ ,  $-COOR^6$ ,  $OCOR^6$ ,  $-CONR^6R^7$ ,  $-R^6NCOR^7$ ,  $-NR^6R^7$ ,  $-CN$ ,  $-NO_2$ ,  $-CX_3$ ,  $-SO_2R^6$ ,  $-SO_2OR^6$ ,  $-SO_2NR^6R^7$ ,  $-R^6NSO_2R^7$ , perfluoroalkyl, lower alkyl, lower alkenyl, lower alkynyl, cycloalkyl, heterocycle and aryl;

$R^3$  is selected from the group consisting of hydrogen, halogen,  $-OR^6$ ,  $-COR^6$ ,  $-COOR^6$ ,  $OCOR^6$ ,  $-CONR^6R^7$ ,  $-R^6NCOR^7$ ,  $-NR^6R^7$ ,  $-CN$ ,  $-NO_2$ ,  $-CX_3$ ,  $-SO_2R^6$ ,  $-SO_2OR^6$ ,  $-$

$\text{SO}_2\text{NR}^6\text{R}^7$ ,  $-\text{R}^6\text{NSO}_2\text{R}^7$ , perfluoroalkyl, lower alkyl, lower alkenyl, lower alkynyl, cycloalkyl, heterocycle and aryl;

$\text{R}^4$  is selected from the group consisting of hydrogen, halogen,  $-\text{OR}^6$ ,  $-\text{COR}^6$ ,  $-\text{COOR}^6$ ,  $\text{OCOR}^6$ ,  $-\text{CONR}^6\text{R}^7$ ,  $-\text{R}^6\text{NCOR}^7$ ,  $-\text{NR}^6\text{R}^7$ ,  $-\text{CN}$ ,  $-\text{NO}_2$ ,  $-\text{CX}_3$ ,  $-\text{SO}_2\text{R}^6$ ,  $-\text{SO}_2\text{OR}^6$ ,  $-\text{SO}_2\text{NR}^6\text{R}^7$ ,  $-\text{R}^6\text{NSO}_2\text{R}^7$ , perfluoroalkyl, lower alkyl, lower alkenyl, lower alkynyl, cycloalkyl, heterocycle and aryl;

$\text{R}^5$  is selected from the group consisting of hydrogen, halogen,  $-\text{OR}^6$ ,  $-\text{COR}^6$ ,  $-\text{COOR}^6$ ,  $\text{OCOR}^6$ ,  $-\text{CONR}^6\text{R}^7$ ,  $-\text{R}^6\text{NCOR}^7$ ,  $-\text{NR}^6\text{R}^7$ ,  $-\text{CN}$ ,  $-\text{NO}_2$ ,  $-\text{CX}_3$ ,  $-\text{SO}_2\text{R}^6$ ,  $-\text{SO}_2\text{OR}^6$ ,  $-\text{SO}_2\text{NR}^6\text{R}^7$ ,  $-\text{R}^6\text{NSO}_2\text{R}^7$ , perfluoroalkyl, lower alkyl, lower alkenyl, lower alkynyl, cycloalkyl, heterocycle and aryl;

$\text{R}^6$  and  $\text{R}^7$  is selected from the group consisting of hydrogen, halogen,  $-\text{OR}^2$ ,  $-\text{CX}_3$ , perfluoroalkyl, lower alkyl, lower alkenyl, lower alkynyl, cycloalkyl, heterocycle and aryl;

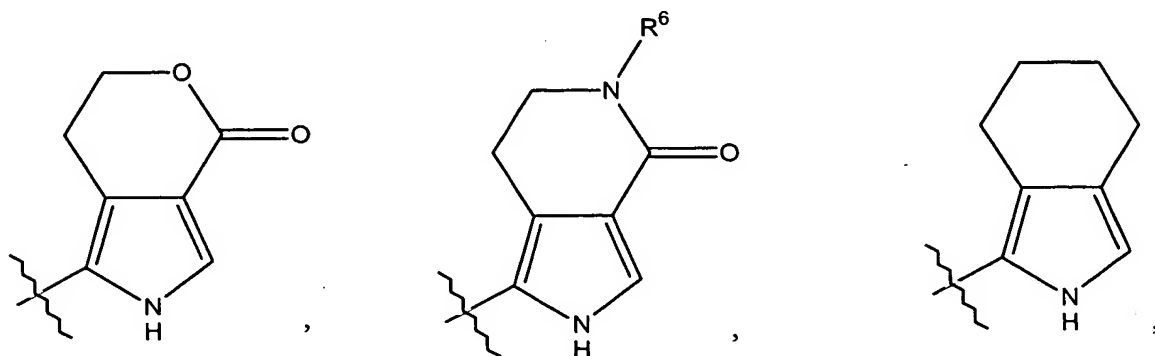
X is fluorine, chlorine, bromine or iodine;

$\text{R}^3$  and  $\text{R}^4$  cannot both be hydrogen; and

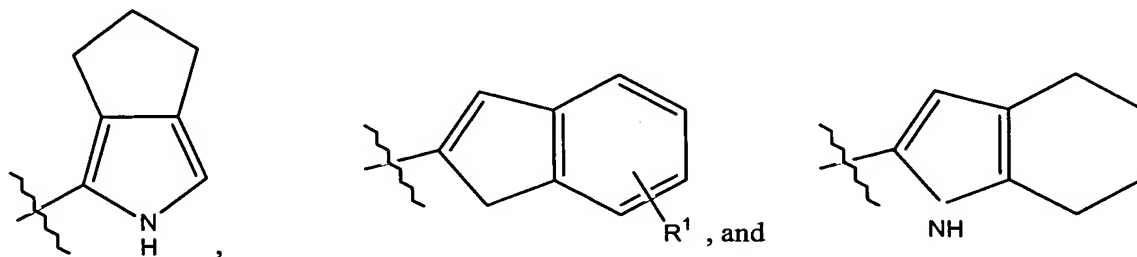
n is 1, 2, 3 or 4,

or a pharmaceutically acceptable salt thereof.

2. The compound of claim 1, wherein  $\text{R}^3$  and  $\text{R}^4$  or  $\text{R}^4$  and  $\text{R}^5$  may be linked together to form a ring.



3. The compound of claim 2, wherein the R<sup>3</sup> and R<sup>4</sup> or R<sup>4</sup> and R<sup>5</sup> are linked together to form a ring, the ring together with pyrrole is selected from the group consisting of:



4. A method of modulating the catalytic activity of a protein kinase comprising contacting said protein kinase with a compound of claim 1, or a pharmaceutically acceptable salt thereof.

5. The method of claim 4, wherein said protein kinase is selected from the group consisting of a receptor tyrosine kinase, a non-receptor tyrosine kinase and a serine-threonine kinase.

6. The method of claim 5, wherein said receptor tyrosine kinase whose catalytic activity is modulated by a compound of this invention is selected from the group consisting of EGF, HER2, HER3, HER4, IR, IGF-1R, IRR, PDGFR $\alpha$ , PDGFR $\beta$ , CSFIR, C-Kit, C-fms, Flk-1R, Flk4, KDR/Flk-1, Flt-1, FGFR-1R, FGFR-2R, FGFR-3R, FGFR-4R, DDR-1, DDR-2 and MET.

7. The method of claim 5, wherein said cellular tyrosine kinase whose catalytic activity is modulated by a compound of this invention is selected from the group consisting of Src, Frk, Btk, Csk, Abl, ZAP70, Fes/Fps, Fak, Jak, Ack, Yes, Fyn, Lyn, Lck, Blk, Hck, Fgr and Yrk.

8. The method of claim 5, wherein said serine-threonine protein kinase whose catalytic activity is modulated by a compound of this invention is selected from the group consisting of CDK2, Raf, NEK and BUB1.

9. A method for treating a protein kinase related disorder comprising administering to an organism in need thereof a therapeutically effective amount of a compound of claim 1, or pharmaceutically acceptable salt thereof.

10. The method of claim 9, wherein said protein kinase related disorder is selected from the group consisting of a receptor tyrosine kinase related disorder, a non-receptor tyrosine kinase disorder and a serine-threonine kinase related disorder.

11. The method of claim 9, wherein said protein kinase related disorder is selected from the group consisting of a MET kinase related disorder, FLK kinase related disorder, a FGFR kinase related disorder, SRC kinase related disorder, a DDR kinase related disorder, and a PDGFR kinase related disorder.

12. The method of claim 9, wherein said protein kinase related disorder is a cancer.

13. The method of claim 12, wherein said cancer is selected from the group consisting of squamous cell carcinoma, astrocytoma, Kaposi's sarcoma, glioblastoma, lung cancer, bladder cancer, head and neck cancer, melanoma, ovarian cancer, prostate cancer, breast cancer, small-cell lung cancer, glioma, colorectal cancer, genitourinary cancer and gastrointestinal cancer.

14. The method of claim 9, wherein said protein kinase related disorder is selected from the group consisting of diabetes, an autoimmune disorder, a hyperproliferation disorder, restenosis, fibrosis, psoriasis, von Heppel-Lindau disease, osteoarthritis, rheumatoid arthritis, angiogenesis, an inflammatory disorder, an immunological disorder and a cardiovascular disorder.

15. The method of claim 9, wherein said organism is a human.

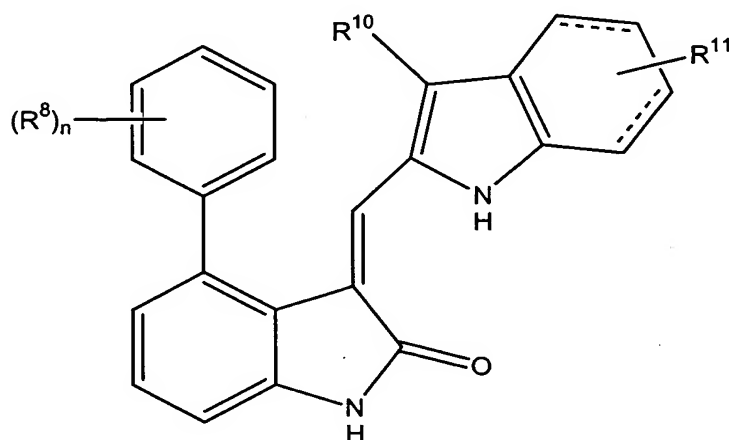
16. A pharmaceutical composition comprising a compound of claim 1 or a pharmaceutically acceptable salt thereof.

17. The pharmaceutical composition of claim 16, which further comprises a pharmaceutically acceptable carrier or excipient.

18. The pharmaceutical composition of claim 16, which further comprises other therapeutic agents.

19. The pharmaceutical composition of claim 18, wherein the other therapeutic agent is selected from the group consisting of an alkylating agent, an antimetabolic chemotherapeutic agent, a natural product based chemotherapeutic agent, mitoxantrone or paclitaxel.

20. A compound of formula III:



wherein each  $R^8$  is independently halogen,  $-OR^6$ ,  $-COR^6$ ,  $-COOR^6$ ,  $OCOR^6$ ,  $-CONR^6R^7$ ,  $-R^6NCOR^7$ ,  $-NR^6R^7$ ,  $-CN$ ,  $-NO_2$ ,  $-CX_3$ ,  $-SR^6$ ,  $-SO_2R^6$ ,  $-SO_2OR^6$ ,  $-SO_2NR^6R^7$ ,  $-R^6NSO_2R^7$ , perfluoroalkyl, lower alkyl, lower alkyl further substituted by one or more of  $R^2$ , lower alkenyl, lower alkenyl further substituted by one or more of  $R^2$ , lower alkynyl, lower alkynyl further substituted by one or more of  $R^2$ , cycloalkyl, cycloalkyl further substituted by one or more of  $R^2$ , a heterocyclic ring, a heterocyclic ring further substituted by one or more of  $R^2$ , aryl and aryl further substituted by one or more of  $R^2$ ;

$R^2$  is selected from the group consisting of hydrogen, halogen,  $-OR^6$ ,  $-COR^6$ ,  $-COOR^6$ ,  $OCOR^6$ ,  $-CONR^6R^7$ ,  $-R^6NCOR^7$ ,  $-NR^6R^7$ ,  $-CN$ ,  $-NO_2$ ,  $-CX_3$ ,  $-SO_2R^6$ ,  $-SO_2OR^6$ ,  $-SO_2NR^6R^7$ ,  $-R^6NSO_2R^7$ , perfluoroalkyl, lower alkyl, lower alkenyl, lower alkynyl, cycloalkyl, a heterocyclic ring and aryl;

$R^6$  and  $R^7$  are independently selected from the group consisting of hydrogen, - $CX_3$ , perfluoroalkyl, lower alkyl, lower alkenyl, lower alkynyl, cycloalkyl, a heterocyclic ring and aryl;

wherein lower alkyl, lower alkenyl, lower alkynyl, cycloalkyl, the heterocyclic ring or aryl may be further substituted by one or more of  $-NR^{12}R^{13}$ , hydroxy, halo, a heterocyclic ring, lower alkyl,  $-C(O)-NR^{12}R^{13}$ ,  $-OR^{12}$ , or  $-SO_2R^{12}R^{13}$ ;

wherein said a heterocyclic ring may be further substituted by one or more of lower alkyl,  $-COR^{12}$ ,  $-NR^{12}COR^{13}$ , halogen,  $-OR^{12}$ ,  $CX_3$ ,  $-C(O)NR^{12}R^{13}$ ,  $-SO_2R^{12}R^{13}$ , or  $-SO_2NR^{12}R^{13}$ ,

or  $R^6$  and  $R^7$  may be linked together to form a 4, 5- or 6- membered ring, optionally containing a hetero atom selected from the group consisting of N, O, S, SO and  $SO_2$ , which may be further substituted by  $CONR^{12}R^{13}$ , lower alkyl, hydroxy,  $-(CH_2)_n-NR^{12}R^{13}$ ,  $-(CH_2)_n$ -heterocycle,  $-(CH_2)_n-C(O)-NR^{12}R^{13}$ ,  $-(CH_2)_n-SO_2R^{12}R^{13}$ , or  $-(CH_2)_n-NSO_2R^{12}R^{13}$ , wherein said heterocycle may be further substituted by lower alkyl,  $-COR^{12}$ , hydroxy,  $-C(O)-NR^{12}R^{13}$ ,  $-OR^{12}$ ,  $-SO_2R^{12}R^{13}$ , or  $-SO_2NR^{12}R^{13}$ ;

X is fluorine, chlorine, bromine or iodine;

$R^{10}$  is H, lower alkyl, lower alkyl substituted with one or more of  $R^2$ ,  $-(CH_2)_nNR^6R^7$ ,  $-CONR^6R^7$ ,  $-SO_2NR^6R^7$ ,  $-(CH_2)_n-SR^6$ ,  $-(CH_2)_n-SOR^6$ ,  $-(CH_2)_n-SO_2R^6$ ,  $-(CH_2)_n-SO_2NR^6R^7$ , or  $-(CH_2)_n-OR^6$ ;

$R^{11}$  is H, lower alkyl, lower alkyl substituted with one or more of  $R^2$ ,  $-(CH_2)_nNR^6R^7$ ,  $-CONR^6R^7$ ,  $-SO_2NR^6R^7$ ,  $-(CH_2)_n-SR^6$ ,  $-(CH_2)_n-SOR^6$ ,  $-(CH_2)_n-SO_2R^6$ ,  $-(CH_2)_n-SO_2NR^6R^7$ , or  $-(CH_2)_n-OR^6$ ;

$R^{12}$  is selected from the group consisting of hydrogen,  $-CX_3$ , perfluoroalkyl, lower alkyl, lower alkenyl, lower alkynyl, cycloalkyl,  $-(CH_2)_n$ -heterocycle, and aryl;

$R^{13}$  is selected from the group consisting of hydrogen,  $-CX_3$ , perfluoroalkyl, lower alkyl, lower alkenyl, lower alkynyl, cycloalkyl,  $-(CH_2)_n$ -heterocycle, and aryl;

or  $R^{12}$  and  $R^{13}$  may be linked together to form a 4-, 5- or 6- membered ring optionally containing one or more hetero atoms selected from the group consisting of O, N, S, SO and  $SO_2$ , which may contain 1 or 2 double bonds; and

wherein ---- is a single or double bond; and

n is 0-4,

or a pharmaceutically acceptable salt thereof.